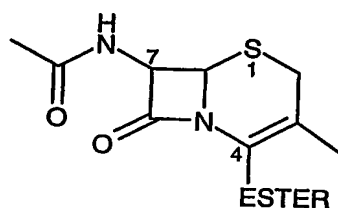


Patent claims:

1. A pharmaceutically active compound having a carboxylic acid group -COOH as a part of its chemical structure which -COOH group is in the form of a carboxylic acid ester and which carboxylic acid ester is selected from the group consisting of
- 1-(2,3-disubstituted 1-propoxycarbonyloxy)-ethyl carboxylic acid ester, wherein the substituents are selected from the group consisting of hydroxy and (C_{1-22}) alkylcarbonyloxy,
 - 1-(1,3-disubstituted 2-propoxycarbonyloxy)-ethyl carboxylic acid ester, wherein the substituents are selected from the group consisting of hydroxy and (C_{1-22}) alkylcarbonyloxy,
 - 1-(9H-fluorene-9-yl- (C_{1-4}) alkanyloxycarbonyloxy)-ethyl carboxylic acid ester,
 - 1-(decahydro-naphthalene-2-yl-oxycarbonyloxy)-ethyl carboxylic acid ester and
 - 1-(2-amino (C_{1-6}) alkoxycarbonyloxy)-ethyl carboxylic acid ester,
- with the proviso that, if the pharmaceutically active compound is a penicillin, then, 1-(2-amino (C_{1-4}) alkoxycarbonyloxy)-ethyl carboxylic acid esters are excluded.

2. A compound of claim 1, wherein the pharmaceutically active compound is a β -lactam antibiotic with the proviso of claim 1.

3. A compound of claim 1, wherein the pharmaceutically active compound is a cephalosporin, e.g. comprising the basic structural elements as set out in formula

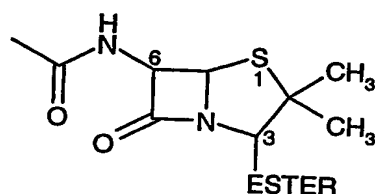


CEPH

wherein ESTER is a carboxylic acid ester as defined in claim 1.

4. A compound of any one of claims 1 or 2, wherein the pharmaceutically active compound is a penicillin, e.g. comprising the basic structural elements as set out in formula

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PENICILLIN

and ESTER is a carboxylic acid ester as defined in claim 1, with the proviso of claim 1.

5. A compound of any one of claims 1 to 4, wherein the $-\text{COOH}$ group is in the form of an ester selected from the group consisting of

- 1-(2,3,-dihydroxy-1-propoxycarbonyloxy)-ethyl-oxy-carbonyl,
- 1-(2,3-diacetoxy-1-propoxycarbonyloxy)-ethyl-oxy-carbonyl,
- 1-(1,3-diacetoxy-2-propoxycarbonyloxy)-ethyl-oxy-carbonyl,
- 1-(2-octanoyloxy-3-acetoxy-1-propoxycarbonyloxy)-ethyl-oxy-carbonyl,
- 1-(2-acetoxy-3-octanoyloxy-1-propoxycarbonyloxy)-ethyl-oxy-carbonyl,
- 1-(9H-fluorene-9-yl-methoxycarbonyloxy)-ethyl-oxy-carbonyl,
- 1-(9H-fluorene-9-yl-ethoxycarbonyloxy)-ethyl-oxy-carbonyl,
- 1-(decahydro-naphthalene-2-yl-oxycarbonyloxy)-ethyl-oxy-carbonyl and
- 1-(2-amino-ethoxycarbonyloxy)-ethyl-oxy-carbonyl, with the proviso of claim 1.

6. A compound of claim 3, wherein the cephalosporin of formula CEPH is selected from the group consisting of

- 7-{2-(5-Amino-[1,2,4]thiadiazol-3-yl)-2-(fluoromethoxyimino)-acetyl-amino}-3-[methyl-(imino-piperazin-1-yl-methyl)-hydrazonomethyl]-8-oxo-5-thia-1-aza-bicyclo[4.2.0]oct-2-ene-2-carboxylic acid,
- 7-{2-(5-Amino-[1,2,4]thiadiazol-3-yl)-2-(fluoromethoxyimino)-acetyl-amino}-3-[[3-ethyl-2-(methylimino)-imidazolidin-1-yl]-hydrazonomethyl]-8-oxo-5-thia-1-aza-bicyclo[4.2.0]oct-2-ene-2-carboxylic acid,
- 7-{2-(5-Amino-[1,2,4]thiadiazol-3-yl)-2-(fluoromethoxyimino)-acetyl-amino}-3-[(carbamimidoyl)-hydrazonomethyl]-8-oxo-5-thia-1-aza-bicyclo[4.2.0]oct-2-ene-2-carboxylic acid,
- 7-{2-(5-Amino-[1,2,4]thiadiazol-3-yl)-2-(fluoromethoxyimino)-acetyl-amino}-3-[(1,4,5,6,-tetrahydropyrimidin-2-yl)-hydrazonomethyl]-8-oxo-5-thia-1-aza-bicyclo[4.2.0]oct-2-ene-2-carboxylic acid,
- 7-{2-(5-Amino-[1,2,4]thiadiazol-3-yl)-2-(fluoromethoxyimino)-acetyl-amino}-3-{methyl-[N-(4-amino-cyclohexyl)-carbamimidoyl]-hydrazonomethyl]-8-oxo-5-thia-1-aza-

bicyclo[4.2.0]oct-2-ene-2-carboxylic acid,

- 7-{2-(5-Amino-[1,2,4]thiadiazol-3-yl)-2-(fluoromethoxyimino)-acetyl-amino}-3-[(2-dimethyl-amino-4,5-dihydro-imidazol-1-yl-imino)-methyl]-8-oxo-5-thia-1-aza-bicyclo[4.2.0]oct-2-ene-2-carboxylic acid,

5 - 3-Carbamoyloxymethyl-7-{2-furan-2-yl-[(Z)-methoxyimino]-acetyl-amino}-8-oxo-5-thia-1-aza-bicyclo[4.2.0]oct-2-ene-2-carboxylic acid, and

- 7-{2-(5-Amino-[1,2,4]thiadiazol-3-yl)-2-(fluoromethoxyimino)-acetyl-amino}-3-[(3-ethyl-2-(methylimino)-imidazol-1-yl-imino)-methyl]-8-oxo-5-thia-1-aza-bicyclo[4.2.0]oct-2-ene-2-carboxylic acid,

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7. A compound of any one claims 1 to 3 selected from the group consisting of

- 7-{2-(5-Amino-[1,2,4]thiadiazol-3-yl)-2-(fluoromethoxyimino)-acetyl-amino}-3-[methyl-(imino-piperazin-1-yl-methyl)-hydrazonomethyl]-8-oxo-5-thia-1-aza-bicyclo[4.2.0]oct-2-ene-2-carboxylic acid 1-(2,3-dihydroxy-1-propoxycarbonyloxy)-ethyl ester,

15 - 7-{2-(5-Amino-[1,2,4]thiadiazol-3-yl)-2-(fluoromethoxyimino)-acetyl-amino}-3-[methyl-(imino-piperazin-1-yl-methyl)-hydrazonomethyl]-8-oxo-5-thia-1-aza-bicyclo[4.2.0]oct-2-ene-2-carboxylic acid 1-(2,3-diacetoxy-1-propoxycarbonyloxy)-ethyl ester,

- 7-{2-(5-Amino-[1,2,4]thiadiazol-3-yl)-2-(fluoromethoxyimino)-acetyl-amino}-3-[methyl-(imino-piperazin-1-yl-methyl)-hydrazonomethyl]-8-oxo-5-thia-1-aza-bicyclo[4.2.0]oct-2-ene-2-carboxylic acid 1-(1,3-diacetoxy-2-propoxycarbonyloxy)-ethyl ester,

20 - 7-{2-(5-Amino-[1,2,4]thiadiazol-3-yl)-2-(fluoromethoxyimino)-acetyl-amino}-3-[methyl-(imino-piperazin-1-yl-methyl)-hydrazonomethyl]-8-oxo-5-thia-1-aza-bicyclo[4.2.0]oct-2-ene-2-carboxylic acid 1-(2-octanoyl-3-acetoxy-1-propoxycarbonyloxy)-ethyl ester,

- 7-{2-(5-Amino-[1,2,4]thiadiazol-3-yl)-2-(fluoromethoxyimino)-acetyl-amino}-3-[methyl-(imino-piperazin-1-yl-methyl)-hydrazonomethyl]-8-oxo-5-thia-1-aza-bicyclo[4.2.0]oct-2-ene-2-carboxylic acid 1-(2-acetoxy-3-octanoyl-1-propoxycarbonyloxy)-ethyl ester,

25 - 7-{2-(5-Amino-[1,2,4]thiadiazol-3-yl)-2-(fluoromethoxyimino)-acetyl-amino}-3-[methyl-(imino-piperazin-1-yl-methyl)-hydrazonomethyl]-8-oxo-5-thia-1-aza-bicyclo[4.2.0]oct-2-ene-2-carboxylic acid 1-(2-aminoethoxycarbonyloxy)-ethyl ester,

30 - 7-{2-(5-Amino-[1,2,4]thiadiazol-3-yl)-2-(fluoromethoxyimino)-acetyl-amino}-3-[methyl-(imino-piperazin-1-yl-methyl)-hydrazonomethyl]-8-oxo-5-thia-1-aza-bicyclo[4.2.0]oct-2-ene-2-carboxylic acid 1-(2,3-dihydroxy-1-propoxycarbonyloxy)-ethyl ester,

- 7-{2-(5-Amino-[1,2,4]thiadiazol-3-yl)-2-(fluoromethoxyimino)-acetyl-amino}-3-[methyl-(imino-piperazin-1-yl-methyl)-hydrazonomethyl]-8-oxo-5-thia-1-aza-bicyclo[4.2.0]oct-2-

- ene-2-carboxylic acid 1-(decahydro-naphthalen-2-yl-oxycarbonyloxy)-ethyl ester,
 - 7-{2-(5-Amino-[1,2,4]thiadiazol-3-yl)-2-(fluoromethoxyimino)-acetylamino}-3-[(imino-piperazin-1-yl-methyl)-hydrazonomethyl]-8-oxo-5-thia-1-aza-bicyclo[4.2.0]oct-2-ene-2-carboxylic acid 1-(2-aminoethoxycarbonyloxy)-ethyl ester,
- 5 - 7-{2-(5-Amino-[1,2,4]thiadiazol-3-yl)-2-(fluoromethoxyimino)-acetylamino}-3-[(imino-piperazin-1-yl-methyl)-hydrazonomethyl]-8-oxo-5-thia-1-aza-bicyclo[4.2.0]oct-2-ene-2-carboxylic acid 1-(decahydro-naphthalen-2-yl-oxycarbonyloxy)-ethyl ester,
 - 7-{2-(5-Amino-[1,2,4]thiadiazol-3-yl)-2-(fluoromethoxyimino)-acetylamino}-3-[methyl-(imino-piperazin-1-yl-methyl)-hydrazonomethyl]-8-oxo-5-thia-1-aza-bicyclo[4.2.0]oct-2-ene-2-carboxylic acid 1-(9H-fluoren-9-yl-methoxycarbonyloxy)-ethyl ester,
- 10 - 7-{2-(5-Amino-[1,2,4]thiadiazol-3-yl)-2-(fluoromethoxyimino)-acetylamino}-3-[methyl-(imino-piperazin-1-yl-methyl)-hydrazonomethyl]-8-oxo-5-thia-1-aza-bicyclo[4.2.0]oct-2-ene-2-carboxylic acid 1-[(1-(9H-fluoren-9-yl)-ethoxycarbonyloxy)-ethyl ester,
 - 7-{2-(5-Amino-[1,2,4]thiadiazol-3-yl)-2-(fluoromethoxyimino)-acetylamino}-3-[[[3-ethyl-2-(methylimino)-imidazolidin-1-yl]-hydrazonomethyl]-8-oxo-5-thia-1-aza-bicyclo[4.2.0]oct-2-ene-2-carboxylic acid 1-(9H-fluoren-9-yl-methoxycarbonyloxy)-ethyl ester,
- 15 - 7-{2-(5-Amino-[1,2,4]thiadiazol-3-yl)-2-(fluoromethoxyimino)-acetylamino}-3-[carbamimidoyl]-hydrazonomethyl]-8-oxo-5-thia-1-aza-bicyclo[4.2.0]oct-2-ene-2-carboxylic acid 1-(9H-fluoren-9-yl-methoxycarbonyloxy)-ethyl ester,
 - 7-{2-(5-Amino-[1,2,4]thiadiazol-3-yl)-2-(fluoromethoxyimino)-acetylamino}-3-[(1,4,5,6,-tetrahydropyrimidin-2-yl)-hydrazonomethyl]-8-oxo-5-thia-1-aza-bicyclo[4.2.0]oct-2-ene-2-carboxylic acid 1-(9H-fluoren-9-yl-methoxycarbonyloxy)-ethyl ester,
- 20 - 7-{2-(5-Amino-[1,2,4]thiadiazol-3-yl)-2-(fluoromethoxyimino)-acetylamino}-3-{methyl-[N-(4-amino-cyclohexyl)-carbamimidoyl]-hydrazonomethyl]-8-oxo-5-thia-1-aza-bicyclo[4.2.0]oct-2-ene-2-carboxylic acid 1-(9H-fluoren-9-yl-methoxycarbonyloxy)-ethyl ester,
- 25 - 7-{2-(5-Amino-[1,2,4]thiadiazol-3-yl)-2-(fluoromethoxyimino)-acetylamino}-3-[(2-dimethylamino-4,5-dihydro-imidazol-1-yl-imino)-methyl]-8-oxo-5-thia-1-aza-bicyclo[4.2.0]oct-2-ene-2-carboxylic acid 1-(2,3-dihydroxy-1-propoxycarbonyloxy)-ethyl ester,
- 30 - 7-{2-(5-Amino-[1,2,4]thiadiazol-3-yl)-2-(fluoromethoxyimino)-acetylamino}-3-[(carbamimidoyl)-hydrazonomethyl]-8-oxo-5-thia-1-aza-bicyclo[4.2.0]oct-2-ene-2-carboxylic acid 1-(2,3-dihydroxy-1-propoxycarbonyloxy)-ethyl ester,
 - 7-{2-(5-Amino-[1,2,4]thiadiazol-3-yl)-2-(fluoromethoxyimino)-acetylamino}-3-[(1,4,5,6,-

- tetrahydropyrimidin-2-yl)-hydrazonomethyl]-8-oxo-5-thia-1-aza-bicyclo[4.2.0]oct-2-ene-2-carboxylic acid 1-(2,3-dihydroxy-1-propoxycarbonyloxy)-ethyl ester,
- 5 - 7-{2-(5-Amino-[1,2,4]thiadiazol-3-yl)-2-(fluoromethoxyimino)-acetylamino}-3-[(2-dimethylamino-4,5-dihydro-imidazol-1-yl-imino)-methyl]-8-oxo-5-thia-1-aza-bicyclo[4.2.0]oct-2-ene-2-carboxylic acid 1-(2,3-dihydroxy-1-propoxycarbonyloxy)-ethyl ester,
- 7-{2-(5-Amino-[1,2,4]thiadiazol-3-yl)-2-(fluoromethoxyimino)-acetylamino}-3-[methyl-(imino-piperazin-1-yl-methyl)-hydrazonomethyl]-8-oxo-5-thia-1-aza-bicyclo[4.2.0]oct-2-ene-2-carboxylic acid 1-(2,3-dihydroxy-1-propoxycarbonyloxy)-ethyl ester,
- 10 - 7-{2-(5-Amino-[1,2,4]thiadiazol-3-yl)-2-(fluoromethoxyimino)-acetylamino}-3-[[3-ethyl-2-(methylimino)-imidazolidin-1-yl]-hydrazonomethyl]-8-oxo-5-thia-1-aza-bicyclo[4.2.0]oct-2-ene-2-carboxylic acid 1-(2,3-dihydroxy-1-propoxycarbonyloxy)-ethyl ester,
- 7-{2-(5-Amino-[1,2,4]thiadiazol-3-yl)-2-(fluoromethoxyimino)-acetylamino}-3-{methyl-[N-(4-amino-cyclohexyl)-carbamimidoyl]-hydrazonomethyl]-8-oxo-5-thia-1-aza-bicyclo[4.2.0]oct-2-ene-2-carboxylic acid 1-(2,3-dihydroxy-1-propoxycarbonyloxy)-ethyl ester,
- 15 - 3-Carbamoyloxymethyl-7-{2-furan-2-yl-[(Z)-methoxyimino]-acetylamino}-8-oxo-5-thia-1-aza-bicyclo[4.2.0]oct-2-ene-2-carboxylic acid 1-(9H-fluoren-9-yl-methoxycarbonyloxy)-ethyl ester, and
- 20 - 3-Carbamoyloxymethyl-7-{2-furan-2-yl-[(Z)-methoxyimino]-acetylamino}-8-oxo-5-thia-1-aza-bicyclo[4.2.0]oct-2-ene-2-carboxylic acid 1-(2,3-dihydroxy-1-propoxycarbonyloxy)-ethyl ester,
- 25 8. A compound of any one of claims 1 to 7 in the form of a salt.
9. A compound of any one of claims 1 to 8 for use as a pharmaceutical.
10. A compound of any one of claims 1 to 8 for the preparation of a medicament for the treatment of microbial diseases.
- 30 11. A pharmaceutical composition comprising a compound of any one of claims 1 to 8 in association with at least one pharmaceutical excipient.
12. A pharmaceutical composition comprising a compound of any one of claims 1 to 8

together with another pharmaceutically active compound.

13. The use of an ester group selected from the group consisting of

5 - 1-(2,3-disubstituted 1-propoxycarbonyloxy)-ethyl carboxylic acid ester, wherein the substituents are selected from the group consisting of hydroxy and (C₁₋₂₂)alkylcarbonyloxy,

- 1-(1,3-disubstituted 2-propoxycarbonyloxy)-ethyl carboxylic acid ester, wherein the substituents are selected from the group consisting of hydroxy and (C₁₋₂₂)alkylcarbonyloxy,

10 - 1-(9H-fluorene-9-yl-(C₁₋₄)alkanyloxycarbonyloxy)-ethyl carboxylic acid ester, and
- 1-(decahydro-naphthalene-2-yl-oxycarbonyloxy)-ethyl carboxylic acid ester
for the improvement of oral resorption of a pharmaceutically active compound.

14. A method for treatment of microbial diseases in a subject in need of such treatment,
15 which method comprises administering to said subject an effective amount of a compound of any one of claims 1 to 8 or a pharmaceutical composition of any one of claims 12 or 13.

15. A pharmaceutical combination for use in a method for treatment of claim 15, comprising
20 at least one compound of any one of claims 1 to 8 to be used concomitantly or in sequence with at least one immunosuppressant, immunomodulatory or anti-inflammatory active agent.

IL/18-Dec-2003